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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/668,508	09/22/2000	Henry E. Young	1304-1-019CIP	1973

7590 04/24/2007  
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EXAMINER
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TON, THAIAN N

ART UNIT	PAPER NUMBER
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1632

MAIL DATE	DELIVERY MODE
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04/24/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/668,508

Applicant(s)

YOUNG ET AL.

Examiner

Thaian N. Ton

Art Unit

1632

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 09 April 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The Notice of Appeal was filed on 09 April 2007. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 14-17.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

*thaien ton*  
THAIAN N. TON  
PATENT EXAMINER

Continuation of 3. NOTE: The proposed claim amendments raise new issues that would require further consideration and search, with regard to 112, 1st, enablement and art. In particular, the amended claims recite that the cells are quiescent in serum free medium, in the absence of an induction agent and do not form tumors in an animal would require a new search and consideration. Newly presented claims are directed to particular stem cell markers that would require new search and consideration.

Continuation of 11. does NOT place the application in condition for allowance because:

Preliminarily, the proposed claim amendments have not been entered, therefore all rejections of record are maintained. The Examiner addresses Applicants' arguments as they pertain to the rejections of record.

1. ODP - The ODP rejection is rendered moot in view of the cancellation of claims 14-17 of the '663 application.

2. 112, 1st paragraph - New Matter. The rejection of record, with regard to the limitation that the cells "do not give rise to functional gametes" is maintained. Applicants argue that ES cells are totipotent cells, and that a pluripotent cell is more limited than a totipotent cells, and that the Young Declaration provided evidence that the instantly-claimed PPELSCs have not been demonstrated to form gametes, Applicants argue that the instantly-claimed stem cells are not capable of forming functional gametes, and thus, this recitation does not introduce new matter into the as-filed disclosure. Applicants have amended the claims to remove this phrase. However, the claim amendments have not been entered, therefore the rejection of record is maintained. It is maintained that the Examiner has provided an art-recognized definition for pluripotent cells, and furthermore, as stated in prior Office actions, it is not an art-recognized property of pluripotent stem cells that they cannot give rise to functional gametes. Finally, the as-filed disclosure provides no guidance to show that the claimed cells do not produce functional gametes. As stated in the prior Office action, the Young Declaration appears to state that the instantly-claimed cells could not form gametes in vitro, which is no indication or guidance with regard to the ability of the cells to form gametes in vivo, thus, the Declaration does not overcome the prior rejection of record.

3. Rejections under §102.

The prior rejection of claims 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Capecchi is maintained for reasons of record. It is reiterated that Applicants have not provided guidance to show that their cells cannot form gametes in vivo, as the Declaration only addresses this limitation in vitro. Furthermore, clearly, ES cells sometimes do, and at other times, do not, contribute to the germline. With regard to Applicants' argument that Capecchi requires the germ line transmission of the target via ES cells, the Examiner responds that Capecchi shows that one must select chimeric mice that have germline transmission, thus, some chimeric mice that are produced from ES cells that do not have germline transmission are examples of cells that are used that do not give rise to functional gametes. Applicants' arguments that their cells could not be used in Capecchi's method to replace genes in progeny of mice is not persuasive. Applicants' claimed cells are not distinguished from Capecchi's ES cells because they fulfill the limitations of the claims with regard to the function and characteristics of the cells, in that Capecchi's cells are capable of self-renewal and differentiate into cells of all three germ layers. There is no requirement for Applicants' cells to fulfill the functions of Capecchi's cells. The Examiner does not address Applicants' arguments regarding the various amendments to distinguish Capecchi's cells (for example, with regard to culture conditions of ES/EG cells, or formation of teratomas) from Applicants' because the claim amendments have not been entered, and are thus, not considered.

Claims 14-16 stand rejected under 35 U.S.C. 102(b) as being anticipated by Piedrahita et al. Applicants argue that their cells are distinct from Piedrahita's in that Piedrahita shows germ line transmission, and that further, Applicants argue that the technology of producing chimeric animals is complex and imperfect and not all cells are successfully transmitted, but Applicants argue that the PGCs of Piedrahita are similar to ES cells because they can form all three germ layers and gametes. Applicants argue that PGCs and ES cells are distinguished from the claimed cells because the claimed cells cannot form gametes and do not contribute to the germ line. Furthermore, Applicants argue that the cells of the instant invention cannot be used in Piedrahita's methods because they cannot be used to generate transgenic progeny animals. These arguments are not persuasive. Applicants' claimed cells are not distinguished from Piedrahita's cells because they fulfill the limitations of the claims with regard to the function and characteristics of the cells, in that Piedrahita's cells are capable of self-renewal and differentiate into cells of all three germ layers, as required by the claims. Furthermore, Piedrahita discuss the possibility of germ line transmission, but do not provide evidence of this. Applicants' arguments regarding the various amendments to distinguish Piedrahita's cells (for example, with regard to culture conditions of ES/EG cells, or formation of teratomas) from Applicants' because the claim amendments have not been entered, and are thus, not considered.

4. Rejections under 103.

Claims 14-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Shambloott when taken with Sambrook et al. Applicants argue as above that Shambloott's cells are PGCs and that they have the ability to colonize the germline. Particularly, Applicants argue that their cells are distinct from ES cells and PGCs because the claimed cells are pluripotent, not totipotent, and that when grown under inducing conditions, the isolated cells do not form gametes, as shown by the Young Declaration. These arguments have been considered, but are not persuasive. It is reiterated that although pluripotent cells have the ability to colonize the germline (as stated by Shambloott, and cited by Applicants), but, the cells also have the ability to differentiate to other cells, as evidenced by the production of chimeric animals. For example, the pluripotent cells can differentiate to a cell of another tissue type, such as a neural cell. The claims do not recite that the instantly-claimed cells can never form functional gametes, merely that they do not. Furthermore although Applicants' cells do not form gametes under "inducing" conditions does not provide evidence that Applicants' cells do not ever form functional gametes, for example, under in vivo conditions. Applicants' arguments regarding the various amendments to distinguish Shambloott's cells (for example, with regard to culture conditions of ES/EG cells, or formation of teratomas) from Applicants' because the claim amendments have not been entered, and are thus, not considered.

Claims 14-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson when taken with Sambrook et al. Applicants argue similarly that Thomson's cells are distinct and nonobvious from the instantly claimed cells, because the cells of Thomson are totipotent and capable of giving rise to all somatic lineages, as well as forming gametes. Applicants argue that the instantly claimed

cells cannot form gametes, and thus are distinct from Thomson's cells. The Examiner responds that there is no art of record that shows that Thomson's cells can give rise to functional gametes, or that their cells are totipotent and can give rise to extraembryonic membranes or tissues. Furthermore although Applicants' cells do not form gametes under "inducing" conditions does not provide evidence that Applicants' cells do not ever form functional gametes, for example, under in vivo conditions. Applicants' arguments regarding the various amendments to distinguish Thomson's cells (for example, with regard to culture conditions of ES/EG cells, or formation of teratomas) from Applicants' because the claim amendments have not been entered, and are thus, not considered.